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## SCIENTIFIC ARTICLE

# Effect of Normal Saline administration on circulation stability during general anesthesia induction with propofol in gynecological procedures - Randomised-controlled study

### Daher Rabadi\* 1

1. Department of Anesthesiology, Jordan University of Science & Technology, Irbid, Jordan Received from Jordan University of Science & Technology, Irbid, Jordan.

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Keywords: Isotonic Solutions; Anesthesia; Propofol; Blood Pressure; Heart Rate.	Abstract Background and objective: To compare the effect of prophylactic administration of normal saline against the hypotensive effect of propofol in female patients booked for gynecological procedures. Method: Sixty nine ASA (I, II) patients were randomly allocated into two groups, group 1 received 5 mL.kg <sup>-1</sup> of 0.9% normal saline 10 minutes before induction, whereas group 2 received nothing (control). Anesthesia was induced with propofol and fentanyl then maintained with propofol and remifentanil. We measured hemodynamic variables pre and post general anesthesia induction. Results: Both groups had significant drops in post induction mean arterial blood pressure (P < 0.001). Also both groups had significant drops in post induction heart rate ((P < 0.02 in sample group and P < 0.001 in control group), and 35% of patients in the control group had more than 25% drop in the pre induction mean arterial blood pressure, compared with only 17% of patients in the caline group (D < 0.04)
	in the saline group (P < 0.04). Conclusion: The prophylactic administration of normal saline could decrease the percentage of patients who had a significant drop in their blood pressure after propofol induction of general anesthesia. © 2013 Sociedade Brasileira de Anestesiologia. Published by Elsevier Editora Ltda. All rights reserved.

### Introduction

Propofol is a rapidly acting intravenous hypnotic agent commonly used for the induction and maintenance of short and ambulatory general anesthesia (GA). It has many advantages over the older hypnotic agents for its rapid acting, short recovery and antiemetic effect. However it is often associated with a decrease in blood pressure, which could be a significant problem in elderly and medically compromised patients.

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Anesthesiologists have attempted different methods to prevent the hypotensive effect of propofol during GA induction, including administration of fluids and prophylactic use of medications with vasoconstriction activity <sup>1-4</sup>.

<sup>\*</sup>Corresponding author: Assistant Professor and anesthesiology consultant. Department of Anesthesiology, Jordan University of Science & Technology, P.O. Box: 3030, Irbid (22110), Jordan.

E-mail: daherrabadi@yahoo.com.au

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Normal saline is a cheap and safe crystalloid fluid that could decrease this undesirable side effect of propofol usage. The study aimed to determine the efficacy of normal saline administration before GA induction against the anticipated hypotensive effect of propofol.

#### Method

After obtaining approval from the hospital ethics committee and informed consent from the patients, 69 female ASA (I, II) patients undergoing elective gynecological procedures were enrolled in this study. Patients did not receive any premedication and were randomized into two groups based on computer generated numbers: group 1 received 5 mL.kg<sup>-1</sup> 0.9% normal saline 10 minutes before induction and group 2 did not receive any fluid. The investigators who collected vital signs from the patients were blinded to the randomization process. Exclusion criteria were age below 18 years and pregnancy.

Blood pressure was measured pre induction and post induction (3 minutes post airway manipulation) using a noninvasive automated method with appropriate-sized cuff at admission area. A 25% drop in mean arterial blood pressure was considered to be significant.

All patients were anesthetized in a standard protocol by a senior anesthesiologist. GA was induced with propofol 1% 2-2.5 mg.kg<sup>-1</sup> over 30 seconds, fentanyl 2  $\mu$ g.kg<sup>-1</sup>, and rocuronium 0.6 mg.kg<sup>-1</sup> to facilitate tracheal intubation. Total intravenous anesthesia (TIVA) started with propofol and remifentanil immediately upon loss of verbal contact with the patients.

The number of patients required for the study was calculated from previous studies <sup>4,5</sup>. Using Altman's nomogram for a study with a power of 0.90, 65 patients would be needed to demonstrate a difference in the mean arterial blood pressure of 15 mm Hg, when the level of statistical significance was set to 5%.

Parametric data were analyzed with t-test. Nonparametric data were analyzed with Mann-Whitney U test. Categorical data were analyzed by chi square test or Fisher's exact test, as appropriate. A P value of less than 0.05 was considered significant.

#### Results

There were 35 patients in group 1 and 34 patients in group 2. The two groups were comparable with respect to age, weight and the physical classification system. Table 1 showed patient characteristic data. There were no statistical differences in baseline blood pressures between the two groups (Table 2).

The mean pre induction arterial blood pressure in the study group was 90 mm Hg  $\pm$  8.8; and dropped to 76 mm Hg  $\pm$  10 after induction. In the control group it was 95 mm Hg  $\pm$  15 and fell to 73 mm Hg  $\pm$  13. These changes were significant (P < 0.001). Furthermore, both groups had significant drops in post induction heart rate (P < 0.02 in sample group and P < 0.001 in control group). Figure 1 summarized these changes.

#### Table 1 Patients' demographic features.

	Sample group (35 patients)	Control group (34 patients)
Age in years (mean $\pm$ SD)	$33\pm13$	$35\pm12$
Weight in kg (mean $\pm$ SD)	$74\pm11$	$72\pm15$
ASA I	24	27
ASA II	11	7

	Sample group	Control group	p-val
Systolic blood pressure, mm Hg (mean $\pm$ SD)	$118.6\pm8.5$	$123 \pm 16.4$	0.2
Diastolic blood pressure, mm Hg (mean ± SD)	$\textbf{76.9} \pm \textbf{7.8}$	$\textbf{76.1} \pm \textbf{9.7}$	0.7

Table 2 - Patients' vital signs at admission.

(mean $\pm$ SD)			
Mean Arterial pressure, mm Hg (mean ± SD)	$\textbf{90.8} \pm \textbf{6.7}$	91.7 ± 11.5	0.7
Heart rate (mean $\pm$ SD)	84 ± 10.1	$\textbf{84.7} \pm \textbf{12.5}$	0.8



**Figure 1** Pre and post induction changes in average mean arterial blood pressure and heart rate in both groups.

Figure 2 showed the percentage of patients who had more than a 25% drop in mean arterial blood pressure after propofol induction. Twelve patients in the control group had a significant drop, compared with only 5 patients in the saline group (P < 0.04).

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40 35 30 25 20 15 10 5 0 Control Sample Percentage of significant drop in mean arterial blood pressure.



#### Discussion

In this prospective randomized study we did not find normal saline administration to be helpful in preventing the drop in blood pressure after propofol induction of GA. Both the studied and control groups had statistically significant drops in average mean arterial blood pressure after propofol induction of anesthesia. However there were statistically significant differences in post induction blood pressure drops between both groups.

Propofol has nearly replaced most of the traditional hypnotic agents. It has many advantages over older medications such as its onset, duration and recovery time, maintenance of anesthesia as well as its anti-emetic property. However, the possible serious side effect of drop in blood pressure is still noted in daily anesthesia practice with propofol <sup>6,7</sup>.

The mechanism of propofol-induced hypotension is probably due to a decrease in systemic vascular resistance secondary to arterial and venous vasodilation and a decrease in myocardial contractility <sup>1,6</sup>. To counteract this effect, sympathomatic medications or fluid infusion can be used.

Many authors have used ephedrine to reverse this effect. Gamlin et al. 2 studied the hemodynamic effects of propofol in combination with ephedrine in forty patients using different doses of ephedrine. They found a dose of 15 mg ephedrine or higher to be effective in reducing the drop of blood pressure during induction with propofol in ASA I patients who underwent gynecological procedures. In another study Michelson et al (1) found ephedrine at 0.2 mg.kg-1 to be superior to 0.1 mg.kg<sup>-1</sup> dose in controlling the reduction in blood pressure and heart rate, however even with this high dose of ephedrine it did not completely abolish the decrease in blood pressure associated with propofol induction. We think ephedrine in such dose could cause serious complications like: vomiting, cerebral infarction and arrhythmias. The use of crystalloid fluid preload to prevent hypotension after propofol induction of anesthesia hasn't been thoroughly evaluated. In fasting patients, fluid administration is more likely to remain intravascular than to be distributed into the interstitial and the intracellular spaces, thus, raising venous return and increasing cardiac output that may attenuate hypotensive effect.

The hypotensive property of propofol is dose dependent <sup>8</sup> and more obvious in elderly patients <sup>9</sup>. There is some evidence that the use of fentanyl with propofol induction may potentiate the hypotensive effect of propofol <sup>10</sup>. These factors are unlikely to bias our results.

Both groups in our study had anesthesia according to standard protocol by one anesthesiologist. There were no significant differences in age as well as propofol, fentanyl and ramifentanil dose between the sample and control group.

Although propofol-induced hypotension is usually well tolerated in patients with stenotic coronary artery disease, <sup>11,12</sup> it may occasionally cause cardiovascular collapse and death <sup>13</sup>. Propofol anesthesia is associated with a significant decrease in cardiac oxygen consumption, and the global myocardial oxygen supply-demand ratio is therefore well-preserved <sup>11,12</sup>. However, despite an increase in the global oxygen supply-demand ratio, arterial hypotension may occasionally lead to local myocardial ischemia in areas supplied by a stenotic artery <sup>11</sup>. Arterial hypotension may also jeopardize cerebral perfusion in patients with a significant stenosis in carotid or intracerebral arteries. These serious complications are definitely more important when the mean arterial blood pressure drop significantly, especially in such medically compromised patients. Vital organs' autoregulation is often maintained within mean arterial blood pressure of 60-160 mm Hg; therefore, any critical drop below this level will be hazardous.

Different authors reported variable results on the effect of propofol on the heart rate. Our data was consistent with Michelsen et al. <sup>1</sup> study where induction of anesthesia with propofol was followed by a decrease in heart rate. In contrast, Gamlin et al. <sup>2</sup> found no effect of propofol on heart rate, whereas Turner et al. <sup>4</sup> found increase in heart rate. These conflicting results can be explained by the different methods of anesthesia maintenance performed in these studies.

In summary, we did not find administration of 0.9% normal saline before propofol induction of GA in gynecological procedures to be valuable in preventing a drop in post induction mean arterial blood pressure. However, it was effective in decreasing the percentage of patients with a significant drop as defined by 25% decrease in pre induction mean arterial pressure.

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